Unusual presentation of more common disease/injury

Tryst and treatment of an unusual case of MDR CNS tuberculosis

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Summary

A case of multidrug resistance central nervous system tuberculosis is described. During the initial 6 months of therapy, intracranial embolic spread of tuberculomas from exudates around the proximal left middle cerebral artery was seen. This phenomenon was reported earlier. Further management, therapeutic considerations, particularly with secondary and tertiary line of antitubercular medication and neuroimaging are discussed.

BACKGROUND

We present a rare case of multidrug resistance central nervous system (MDR CNS) tuberculosis, with an unusual mechanism of spread. Further, there was clearance and reappearance of tuberculomas, which may suggest one of the features of MDR CNS tuberculosis on neuroimaging. Finally, the treatment lasted beyond 5 years.

CASE PRESENTATION

A 42-year-old bank employee was hospitalised in February 2006 with a 4 week history of headaches, evening rise in temperature and anorexia. Two weeks prior to admission, he had vomiting once or twice a day along with transient diplopia.

Examination on admission showed that he was mildly emaciated. Vitals and general examinations were normal. Neurological examination did not show any deficits or lateralising signs, but he had neck rigidity with a positive kerning's. Fundus was normal. MRI of the head with contrast showed multiple small enhancing lesions in the cerebellum, with a likelihood of tuberculomas (figure 1A, below). Cerebrospinal fluid examination showed raised pressures, and laboratory analysis showed 125 mg% proteins, 110 cells, 95% lymphocytes and 30 mg% glucose. Cultures grew acid-fast bacilli, resistant to isoniazid and rifampicin.

TREATMENT

The patient was started on tab pyrazinamide 750 mg twice daily, tab levofloxacin 500 mg twice daily, tab ethambutol 1000 mg once daily and inj streptomycin 750 mg, intramuscular once daily. Due to his toxic state, he also took tab prednisolone 40 mg once a day that was tapered off over the next 6 weeks. A month after discharge, an MRI head with contrast was repeated due to exacerbation of headaches. It showed exudates surrounding the proximal part of the left middle cerebral artery (MCA) (figure 1B, top). The headache settled on modest increment of steroids (10 mg). The patient was readmitted in August, the same year, with severe headache followed by seizures that led

to right-sided weakness (power grade 3), and non-fluent aphasia. MRI head with contrast done this time showed clearance of the cerebellar lesions, but continued to show the earlier exudates encasing the proximal MCA. Multiple tuberculomas in the left MCA territory believed to be embolic were seen (figure 1B, below). No stenosis or focal vasculitis of the MCA was seen. This phenomenon was reported earlier, as the first documentation of intracranial spread of tuberculomas by arterial embolisation.¹ Further therapy of this case, till clearance of all lesions in May 2011, is as shown in table 1.

OUTCOME AND FOLLOW-UP

As mentioned in the discussion, the lesions took more than 5 years to clear. Therapeutic management has been shown in table 1, and is also a part of the discussion as well.

DISCUSSION

The case is interesting for its initial presentation, mechanism of relapse and the prolonged therapy required for a complete clearance of lesions. The feature of meningitis along with posterior circulation tuberculomas (figure 1A,

Table 1 MRI pictures showing, presentation, spread and clearance of infection

Drug	Dose	Schedule
Inj Kanamycin	750 mg intramuscularly	Initially given for 6 months then repeated subsequently for 3 months with 3 months gap
Tab Pyrazinamide	750 mg	Given once daily for the first 3 years
Tab Ethionamide	250 mg	Given twice a day for 9 months in subsequent years, with 3 months gap
Tab Cycloserine	250 mg	Given twice a day for 9 months each year with a gap of 3 months
PAS granule		
1) First year	5 g	Given twice daily
2) Second year	5 g	Given twice a day, every alternate day
3) Third year onwards	5 g	Given twice a day, three times a week

PAS, para-aminosalicylic acid.

Figure 1 (A) Shows posterior fossa tuberculomas on presentation (below), but not spread anteriorly (top). (B) Exudates encasing the proximal left MCA (top), and spread via embolisation in the MCA territory (below). (C) Residual tuberculomas, as in an MRI done in November 2010 (top), and clearance, in the MRI done in May 2011 (below).

below) has been observed in other cases of MDR CNS tuberculosis (personal observations, under compilation). In terms of therapy, after a fulminant spread through arterial embolisation within 6 months of start of therapy, the patient was largely managed on secondary and tertiary drugs such as cycloserine, ethionamide, para-aminosalicylic acid granules and inj kanamycin (table 1). The therapy was guided by clinical follow-ups every 3 months, response seen on MRIs done every 6 months, monitoring of liver functions, ototoxicity and any other side effects. The response in the regression of lesions was slow. Hepatic toxicity, manifested as anorexia and raised liver enzymes, was seen on three occasions. The therapy was with held each time for a period between 1 and 2 weeks. At any given time, the patient was on at least three drugs. The pattern of overall therapy and drug combinations that emerged can best be stated to be a result of balancing caution and therapeutic aggression to treat the infection.

Anterior spread (figure 1A, top) was not present initially. The relapse was seen by spread of exudates to another area, and finally intracranial arterial embolisation (figure 1B, top and below). As therapy continued, significant clearance of lesions was seen in November 2010 (figure 1C, top). Complete clearance was seen in May 2011 (figure 1C, below). The total duration of this therapy is a little more than 5 years. Comparable duration of treatment has been reported in patients with pulmonary MDR tuberculosis. Immunocompromised cases were not included in this series.²

Although there are guidelines on antitubercular therapy in MDR tuberculosis in general,³ there is no strict regimen prescribed for CNS MDR tuberculosis. The case is an example of the leverage that may have to be exercised in shuffling the drugs presently classified in the secondary and tertiary category. We are enlisting the final therapy including changes that had to be made due to toxicity and compliance (table 1). We emphasise that this can best be

said to be a combination based on response, side effects, and patient compliance. Being a CNS infection, a slow response was expected. The therapy finally stretched beyond 5 years, even as his clinical and MRI state continued to show a gradual response.

The case suggests some features on neuroimaging that may raise suspicion of MDR CNS tuberculosis. Therapeutic derivations are that secondary and tertiary drugs may have to be used for long periods, the actual combinations varying with the response, tolerance and compliance. Finally, it is the gratifying clearance of the lesions that justifies, and may even suggest prolonged therapy in responsive patients.

We presume, with the compilation of more such cases, early identification on neuroimaging, further guidelines may be laid in the treatment of MDR CNS tuberculosis. Trials of other antibiotics that are effective in the treatment of tuberculosis can never be overstated.⁴ MDR CNS tuberculosis presently has a threat to emerge as a fatal infection, if not treated aggressively, in endemic areas, and in patients with compromised immunity.

Learning points

- Early suggestions of neuroimaging of MDR CNS tuberculosis.
- So far the only case report showing intracranial spread by embolisation via an intra cranial artery.
- Perhaps the only case of MDR CNS tuberculosis that took more than 5 years of treatment. The lesions finally cleared.

Competing interests None.

Patient consent Obtained.

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